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## High resolution bone mineral densitometry with a gamma camera

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**Abstract.** A technique is described by which the regional distribution of bone mineral can be determined in bone samples from small animals. The technique employs an Anger camera interfaced to a medical computer. High resolution (<1 mm) imaging is possible by producing magnified images of the bone samples. Regional densitometry of femurs from oophorectomised and bone grafted rats demonstrated significant heterogeneity of bone mineral loss.

### 1. Introduction

A number of human and animal studies have shown that bone loss associated with disease, immobilisation, bedrest, and weightlessness is not uniformly distributed over the skeleton or even along the length of the individual bones (Yagadovsky *et al* 1976, Johnston and Dietlein 1977, Krolner *et al* 1980, Verhas *et al* 1980). There is evidence that in some disease states early changes involve trabecular bone and only later are changes in compact bone seen (Nordin 1973, Krolner *et al* 1980, Riggs *et al* 1981). Since the large majority of the skeletal mass is composed of compact bone, early bone changes are best detected by methods capable of analysing skeletal bone regions with large trabecular bone content. The development of the dual-photon spine scanner and isotopic and x-ray tomographic densitometer scanners are examples of this effort (Genant and Boyd 1977, Riggs *et al* 1981, Ruegsegger *et al* 1981). It is believed that techniques which can quantitatively measure regional change in bone mineral in the rat or other research animals will be more sensitive than techniques that analyse entire limbs. The purpose of this paper is to describe a technique for quantifying regional bone mineral of rat bones, and to demonstrate in two different rat models where regional loss of bone was apparent while total mineral content was only minimally altered.

### 2. Regional bone mineral technique

Single photon densitometry is an accepted technique for measuring bone mineral. The use of a gamma camera for trans-imaging bone allografts has been described (Strash and Bright 1976). Our method uses a conventional large field of view Anger camera (GE Maxi II) interfaced to a computer (GE Med IV). A wooden jig was built to hold reproducibly a collimated iodine-125 source, bone samples and a lead mask. Figure 1 is a line drawing of this device seated on top of the uncollimated camera head. A

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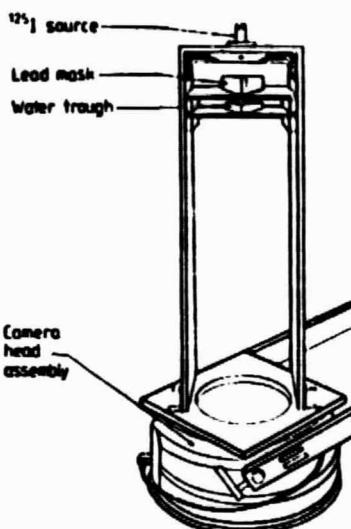


Figure 1. Diagram of apparatus used to obtain bone mineral images.

lead mask is placed on the detector head covering the outer 5 cm of the crystal to eliminate edge packing effects. The  $^{125}\text{I}$  source, about 0.6 mm in diameter, is contained in a lead shield with a 5 mm hole serving as a collimator. The  $^{125}\text{I}$  source strength varied over a 10 month interval from 814 to 26 MBq. Tin filters are placed in front of the collimator port to reduce the gamma count rate at the camera to about 20 000 cps. A 35% window centred about the  $^{125}\text{I}$  photopeak is used. Immediately above the bone sample a lead mask is positioned which limits the x-ray beam to the approximate area of the bone, further reducing camera count rate and scattered radiation. Immediately below the lead mask, the bone sample is placed in a water trough. Positioning the specimen is easily achieved by trans-imaging the sample while viewing the camera persistence scope. The source-to-bone and source-to-camera distances are 20 and 157 cm, respectively. Initially, with the water trough in place but without the mask, a  $5 \times 10^6$  count flood is obtained which is used to correct for uniformity all subsequent images. Bone images of  $3 \times 10^6$  counts are collected, flood corrected and stored in a  $64 \times 64$  matrix. A 0.3 g piece of aluminium which has an attenuation similar to rat bone is imaged with each set of bones to check system stability.

Typically, the stored images are processed line by line, one pixel width wide, to obtain regional bone mineral. Each pixel corresponds to a 0.91 mm square at the sample position. The standard assumptions of single photon absorptiometry were made, namely, that a monoenergetic beam is attenuated by a two compartment system of constant total thickness. The relative bone mineral thickness per pixel is  $\ln(I_0/I)$  where  $I_0$  and  $I$  are the intensities in the background region and the pixel being measured respectively.

Integrating the thickness per pixel over one dimension gives the bone mineral thickness along this line, while integration over two dimensions of this distribution gives the total bone mineral content of the bone. In order to examine linearity, the attenuation by three pieces of Al of approximately equal area but different thicknesses was measured. The weights of the aluminium were 0.141 g, 0.294 g and 0.461 g. Figure 2 is a plot of relative Al weight against relative density. The correlation coefficient was 0.99. The Al sample, with a relative weight of 2.1 (0.3 g) and an

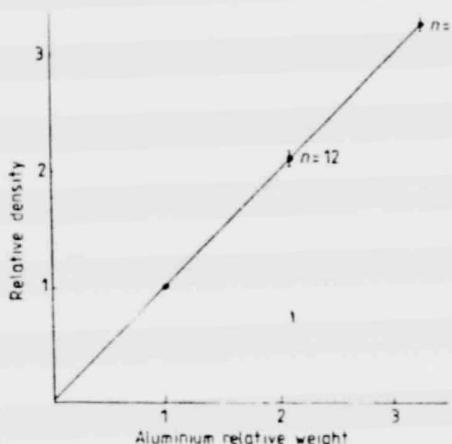


Figure 2. Plot of relative density against relative aluminium weights. Error bars are the standard deviation for indicated number of measurements.

attenuation comparable to that of the rat bones, was measured twelve times over a nine month period. The per cent standard deviation of these measurements was 4.8%.

In order to determine resolution, a bar phantom consisting of sets of equally spaced lines was imaged. Because the resolution of the sample position was less than the largest bar spacing, the phantom was imaged about 6 cm closer to the source than the usual sample position. The actual resolution was determined by correcting the observed bar resolution by the magnification factor (1.4). Figure 3 shows a photograph of the bar phantom in which a minimum bar spacing of 0.6 mm is observed giving a resolution of approximately 0.8 mm at the standard sample position.

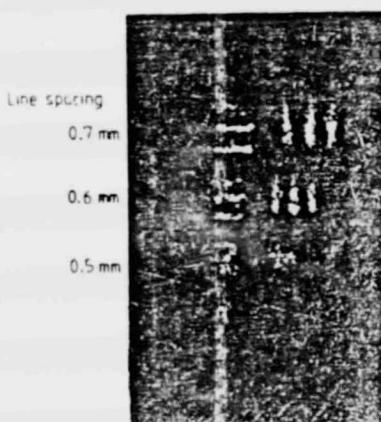


Figure 3. Transmission image of a bar phantom showing spatial resolution. The magnification factor compared with that at the standard sample position is 1.4 so that the resolution at the sample position is about 0.8 mm.

### 3. Oophorectomised rats

In this study 20 female Sprague-Dawley rats were used. The rats were six months of age at the beginning of the study. Ten of the animals were oophorectomised while the other ten served as controls. The animals were fed and watered *ad libitum*. After

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six months the animals were sacrificed, and the left femurs were removed and cleaned of most soft tissue. The bone mineral was measured in 1 mm increments from the knee joint to a point approximately 2 cm proximal to the knee. A mean and standard deviation was obtained at each line for each group. The two groups are compared in figure 4. Two of the oophorectomised rats died before the end of the study and are

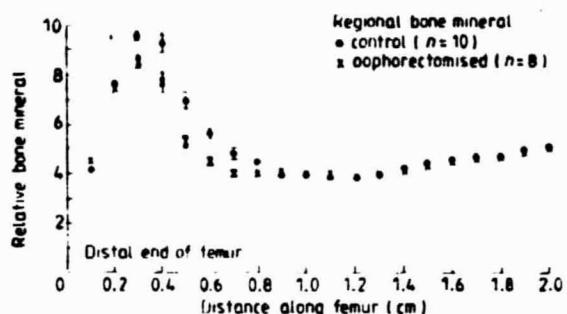


Figure 4. Bone mineral plotted against distance along the femur of controls and rats oophorectomised six months previously. Errors bars are standard errors of the mean.

therefore not included in the calculated means. Integrating the area under the two curves from 0.2 cm to 0.8 cm demonstrated a 15% ( $p < 0.001$ ) relative loss of bone mineral in oophorectomised rats. This portion of the femur contains a large volume of trabecular bone. The total calcium content of entire limbs, measured by neutron activation, showed only a minimal difference between oophorectomised and control animals. The femurs from the oophorectomised animals had an average of 4% less calcium as compared with controls, indicating a selective regional loss of trabecular bone mineral. X-rays of the oophorectomised femurs also indicated a reduction of trabecular bone compared with the controls.

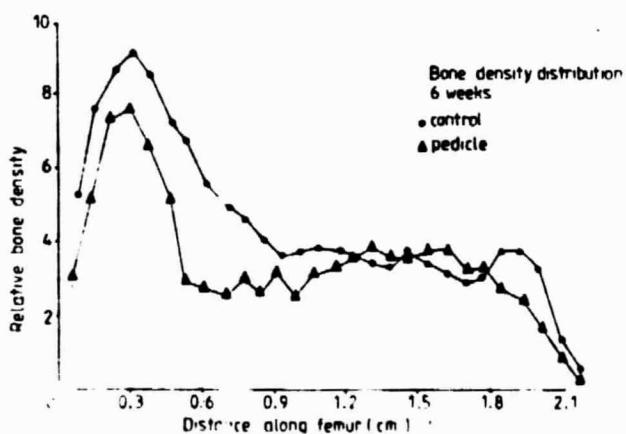


Figure 5. Bone mineral in a rat femur transplanted six weeks prior to sacrifice compared with a similar section of the opposite femur. There is a relative demineralisation of the pedicled bone in the epiphyseal region, particularly in the area below the epiphyseal plate

#### 4. Pedicled bone graft

The free bone pedicle graft is a model developed for the study of chronically immobilised rat bone. In this model, the entire inferior half of the femur is dissected free of tendons and muscle while preserving the nutrient vessel and nerve. The distal 1.5–2.0 cm portion of the femur is then sectioned and transplanted to the groin retaining vascularisation by the femoral vessels. Figure 5 shows the relative bone mineral in the pedicled bone compared to that of the non-immobilised opposite femur in the same animal six weeks after surgery. The pedicled femur shows a mineral loss in the epiphyseal region similar to that seen in the six-month oophorectomised rats. The distal end of the bone up to 0.9 cm shows a 23% decrease in mineral while the remainder of the bone shows an 8% decrease in bone mineral. Figure 6 is a plot of pedicled against control bone six months after surgery. This graph demonstrates a generalised decrease in bone mineral over the length of the bone compared with the localised loss seen in the previous six-week graph.

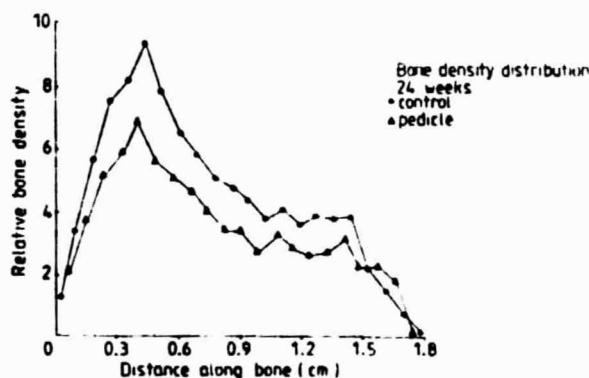


Figure 6. Bone mineral in a rat femur transplanted six months prior to sacrifice compared with a similar section of the opposite femur. This shows generalised demineralisation over the length of the bone

#### 5. Discussion and conclusions

Gamma cameras interfaced to computers are available in most large hospitals. By producing a magnified image of the bone specimen, resolution of the order of 1 mm or less is possible even though intrinsic camera resolution is of the order of 3–4 mm. Since the equipment is readily available, this technique can be implemented at a relatively low cost. The two examples presented show that rat bone is lost non-uniformly and that regional measurements may provide additional useful information over total mineral measurements as well as increasing the sensitivity to detect change.

This technique would be useful in many research studies where quantitation of bone mineral is required.

#### Résumé

Densitométrie haute résolution de l'os minéral.

Les auteurs décrivent une technique permettant de déterminer la distribution régionale de l'os minéral dans des échantillons d'os de petits animaux. Cette technique utilise une caméra d'Anger connectée à un calculateur. Il est possible d'obtenir une haute résolution (< 1 mm) en produisant des images agrandies des

échantillons. La densitométrie régionale de fémurs de rats ovariectomisés, et ayant subi une greffe d'os, montre une hétérogénéité significative dans la perte d'os minéral.

### Zusammenfassung

Hochauflösende Densitometrie von Mineralstoffen im Knochen.

Beschrieben wird ein Verfahren, durch das die regionale Verteilung von Mineralstoffen in Knochenproben kleiner Tiere bestimmt werden kann. Bei dem Verfahren wird eine Anger-Kamera mit angeschlossenem Rechner system verwendet. Abbildungen mit hoher Auflösung (<1 mm) sind möglich durch die Erzeugung vergrößerter Bilder der Knochenproben. Die regionale Densitometrie der Oberschenkelknochen von Ratten nach Oophorektomie und Knochenverpflanzung zeigte eine signifikante Heterogenität bezüglich des Mineral stoffverlustes der Knochen.

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